

### **REMARKS**

Claims 1-6 are pending in the application. Claims 1-3 stand rejected under 35 U.S.C. § 103(a) for obviousness over the Hicke et al. article in view of U.S. Patent No. 4,163,714 to Gregor. Claims 4-6 are rejected under U.S.C. § 103(a) for obviousness over the Hicke article in view of the Gregor patent and in further view of U.S. Patent No. 6,017,742 to Takenishi et al. Applicants respectfully traverse these rejections for the following reasons.

Applicants have already clearly established on the record that the Hicke article only considers a process of functionalizing the surface of capillary-pore membrane transmembrane passageways prior to immobilization of another species thereon. Moreover, the present application references the Hicke article at paragraph [0007] and distinguishes the two-step process for altering the properties of a capillary-pore membrane from the present invention.

This was also acknowledged by the Examiner at least at page 3 of the Office Action, which states “Hicke fails to explicitly disclose that such method only uses endogenous carboxyl groups inherent within one or more transmembrane passageways.” However, the comment in the Office Action that functionalizing capillary-pore membranes with additional carboxyl groups creates an “endogenous” final product is not understood. An endogenous feature is one that is present or derived from an original state. A treatment of a product to add a feature (carboxyl groups) does not make that feature endogenous. Therefore, Hicke’s process cannot be considered to use endogenous carboxyl groups. In order to account for the failure of the Hicke article to disclose endogenous carboxyl groups within one or more transmembrane passageways, the Office Action cites to the Gregor patent.

Gregor discloses modifying polymeric membrane filters to include ligands. During filtration of a mixture, the ligands bind to polymeric material of the filter complex with components in the mixture. The ligands may be provided in the filter polymer as (1) part of the original matrix polymer used in making the membrane; or (2) when placed into the pores, i.e., non-endogenous. That teaching is not combinable with the disclosure of Hicke and, even if attempted, would not result in the present invention.

Firstly, the Office Action states that it would have been obvious to modify the method of Hicke (functionalize a membrane with carboxyl groups and immobilize a binding

species on the carboxyl groups) with Gregor (produce a membrane with a polymer incorporating a ligand). Applicants respectfully disagree. The teachings of Gregor are not combinable with the Hicke article. Hicke clearly only considers a process of first functionalizing the surface of the capillary-pore membrane transmembrane passageways, followed by immobilizing another species thereon. In contrast, the Gregor patent discloses a ligand that is incorporated in the polymeric material used to produce the membrane from the outset. These two teachings are not combinable since one is directed to a multistep process of attaching functional groups and immobilizing other species thereon (Hicke) and the other is directed to polymer membranes having ligands incorporated therein (Gregor). Since Hicke requires a functionalizing step to create an attachment location within membrane pores followed by an attaching step to attach a species for binding to components in a filtration mixture, it would be counter to its teachings to incorporate a binding species throughout the membrane material as opposed to within the pores only. Since their teachings are quite distinct, there is no rationale for their combination.

Neither the Hicke article nor the Gregor patent considers using endogenous binding groups (carboxyl groups) only within the transmembrane passageways of a capillary-pore membrane. The combination of these teachings is inappropriate and would not result in the present invention.

Secondly, the claimed invention provides a method of linking a compound to a membrane only via endogenous carboxyl groups within the transmembrane passageways. This feature is borne out in Example 1. When a membrane without pores was tested for binding of a dye to carboxyl groups, no dye was retained by the membrane. (See Table 1 and paragraphs [0070], [0072].) However, upon creating capillary pores (sized 0.08  $\mu\text{m}$  – 10  $\mu\text{m}$ ), dye was retained. The membranes with the smallest pore diameter (0.08  $\mu\text{m}$ ) bound the most dye, having the highest internal surface area of the pores as compared to the membranes with larger pore diameters. The faces of the membrane without pores did not bind dye to any substantive level, thereby showing that the carboxyl groups within the pores (not the membrane surfaces) are responsible for the binding.

In contrast, membranes produced from polymer incorporating ligands therein (as in Gregor) necessarily have binding sites (the ligands) over the entire membrane – faces and

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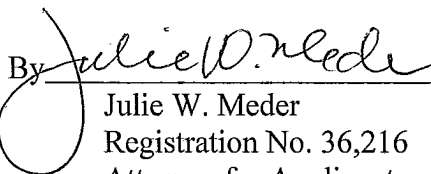
pores – since the ligands are part of the original matrix polymer of Gregor, 2:66-3:1. A membrane produced according to Gregor would not result in binding only within the pores. In other words, the membrane of Gregor does not discriminate between the ligands on its faces and the ligands within the pores.

The method of the present invention links compounds only via endogenous carboxyl groups with the transmembrane passageways. Thus, since Gregor's teachings do not result in binding sites only within the pores, its teachings, even if combined with those of Hicke, could not result in the present invention.

Accordingly, a *prima facie* case of obviousness under 35 U.S.C. § 103(a) has not been established. The teaching of the Takenishi patent relating to reaction of carboxyl groups does not account for the basic failure of the Hicke article taken with the Gregor patent to provide any rationale or ability to modify their teachings to practice the present invention.

Withdrawal of the rejections and allowance of claims 1-6 are respectfully requested.

Respectfully submitted,  
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